

CLAIMS

1. A method of identifying a compound that decreases or inhibits site-1 protease promoter activity, the method comprising:

5 providing a cell comprising a recombinant construct comprising a promoter sequence operably linked to a reporter gene, wherein the promoter sequence comprises (a) the nucleotide sequence set forth as SEQ ID NO:2, or a fragment thereof exhibiting site-1 protease promoter activity, or (b) a nucleic acid sequence that exhibits site-1 protease promoter activity and hybridizes to SEQ ID NO:2 under 10 conditions of hybridization in 0.5 M NaHPO₄, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at 65°C, and washing in 0.1 x SSC/0.1% SDS at 68°C;
15 contacting the cell with a candidate agent;
assaying expression of the reporter gene in the cell; and
determining whether the candidate agent decreases or inhibits expression of the reporter gene, as compared to control level of expression of the reporter gene in the cell in the absence of the candidate agent, wherein a decrease or inhibition of expression of the reporter gene indicates that the candidate agent is a compound that decreases or inhibits site-1 protease promoter activity.

20 2. The method of claim 1, wherein the promoter sequence comprises the nucleotide sequence set forth as SEQ ID NO:2, or a fragment thereof exhibiting site-1 protease promoter activity.

25 3. The method of claim 1, wherein the promoter sequence comprises the nucleotide sequence set forth as SEQ ID NO:1.

4. The method of claim 1, wherein the promoter sequence comprises the nucleotide sequence set forth as SEQ ID NO:2.

30 5. The method of claim 1, wherein the promoter sequence comprises a nucleic acid sequence that exhibits site-1 protease promoter activity and hybridizes to SEQ ID

NO:2 under conditions of hybridization in 0.5 M NaHPO₄, 7% SDS, 1 mM EDTA at 65°C, and washing in 0.1 x SSC/0.1% SDS at 68°C.

6. The method of claim 1, wherein the reporter gene encodes luciferase, beta-
5 galactosidase, alkaline phosphatase, or green fluorescent protein.

7. The method of claim 1, further comprising contacting the cell with insulin, a glitazone, or a sterol prior to assaying expression of the reporter gene.

10 8. The method of claim 1, wherein the candidate agent is an organic molecule, a peptide, a protein, or an oligonucleotide.

15 9. The method of claim 1, further comprising determining whether the compound is effective, in an individual, for treating a medical condition related to obesity.

10. The method of claim 9, wherein the medical condition is obesity.

11. The method of claim 9, wherein the medical condition is type II diabetes.

20 12. The method of claim 9, wherein the medical condition is a cardiovascular disease or dyslipidemia.

25 13. The method of claim 9, wherein the medical condition is hypercholesterolemia or atherosclerosis.

14. A method of identifying a compound that binds to the site-1 protease promoter, the method comprising:

providing a nucleic acid comprising the nucleotide sequence set forth as SEQ ID NO:2, or a fragment thereof exhibiting site-1 protease promoter activity;

5 contacting the nucleotide sequence with a candidate agent; and

determining whether the candidate agent binds to the nucleotide sequence or the fragment thereof, to thereby identify a compound that binds to the site-1 protease promoter.

10 15. The method of claim 14, wherein the nucleic acid comprises the nucleotide sequence set forth as SEQ ID NO:2, or a fragment thereof exhibiting site-1 protease promoter activity.

15 16. The method of claim 14, wherein the nucleic acid comprises the nucleotide sequence set forth as SEQ ID NO:1.

17. The method of claim 14, wherein the nucleic acid comprises the nucleotide sequence set forth as SEQ ID NO:2.

20 18. The method of claim 14, wherein the candidate agent is an organic molecule, a peptide, a protein, or an oligonucleotide.

25 19. The method of claim 14, further comprising determining whether the compound is effective, in an individual, for treating a medical condition related to obesity.

20. The method of claim 19, wherein the medical condition is obesity.

21. The method of claim 19, wherein the medical condition is type II diabetes.

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22. The method of claim 19, wherein the medical condition is a cardiovascular disease or dyslipidemia.

23. The method of claim 19, wherein the medical condition is hypercholesterolemia or atherosclerosis.

5 24. The method of claim 1, further comprising manufacturing the compound as a medicament.

25. The method of claim 14, further comprising manufacturing the compound as a medicament.